

# Biochemistry



David Harris, MD, PhD

## ▶ A Department on the Move

Looking to cure cancer? Want to help stem the tide of obesity and diabetes? Want to find out why some people suffer cardiovascular disease and others grow old with a healthy heart? Some of the answers to these questions are very likely to be found in the research labs of biochemists and molecular and cell biologists.

“Biochemistry as a discipline has evolved significantly over the past 70 years from its origins in attempts to catalogue the molecular parts of living organisms,” says David Harris, MD, PhD, professor and chair of BUSM’s biochemistry department. “Today, biochemistry can encompass virtually any study of biological processes at the cellular or molecular level. Pick up a copy of any of the major scientific journals, and you will find that the papers it contains utilize biochemical techniques.”

The encompassing nature of the field is reflected in the department’s faculty—who are committed to educating the medical, dental, and master’s students throughout the Medical Campus—and the areas of research they pursue. Established in 1935, the department’s research in molecular and cell biology and genetics has had major implications for cardiovascular and pulmonary diseases, cancer, metabolic diseases, and neurodegenerative diseases.

“Perhaps our most important resource is the people in our department, including 30 faculty members, more than 60 graduate students and post-doctoral fellows, and 15 staff members,” says Dr. Harris. “Our work is characterized by extensive interactions within the department and with other basic science and clinical departments at the medical school.”

“We are ranked nationally among the top tier of departments of biochemistry in terms of NIH funding, and we have a long history of making pathbreaking contributions to key areas of biochemistry and molecular biology,” he adds.

Since assuming the role of chair in 2009, Dr. Harris has been on a mission to move the department to even greater achievements by building on its significant strengths and developing new resources, both human and operational. Greater opportunities for collaboration with other departments, programs, and centers on the Medical Campus are leading to increased multidisciplinary research projects.

To expand the research portfolio of the department, he has recruited four new assistant professors in the past two years, a major accomplishment for a basic science department. “This has been an incredibly fun part of my job,” he says. “Learning about whole new areas of biology and identifying young scientists at the cutting edge was incredibly exciting for me and all the members of our superb search committee.”

One new faculty member, cellular and molecular biologist Xaralabos Varelas, PhD, works on signaling pathways that regulate cell size, which has important implications for understanding the growth and development of tissues and organs, and how the underlying pathways go awry in cancer and lead to tumor metastasis. Valentina Perissi, PhD, a biochemist and cell biologist, studies transcriptional control and the assembly of regulatory complexes on DNA. Her most recent findings have important implications for inflammation and diabetes. Mikel Garcia-Marcos, PhD, a biochemist, examines G proteins, which are gatekeepers of cell signaling and regulate virtually any physiological process, and dysregulation of their function (the cause of many diseases). Brigitte Ritter, PhD, a cell biologist, is studying the mechanisms of intracellular trafficking that have direct connections to diseases such as Alzheimer’s disease.

“From the outset, David’s [Harris] purpose has been to bring people in to fit into growing areas so we as a department can grow through those individuals,” says Stephen Farmer, PhD, professor of biochemistry and a member of the department for more than 30 years. “He has looked at not just the future of the department but of science.”

A highly accomplished molecular biologist, Farmer is also a leading researcher on obesity. His lab has focused on identifying the mechanisms that regulate adipose tissue—or fat cell—formation and function. “Bringing in Valentina [Perissi] provides new blood and new perspective on this growing area of research as the rise in obesity is associated with the dramatic increase in diabetes and cardiovascular disease, among others,” he says.

“An extremely important part of understanding how cells work is understanding how certain genes are turned

**FEATURE** “The key to finding cures for the most serious human illnesses lies in understanding how the business of biochemistry. It is an incredibly exciting time in our field, with the advent of major

molecular pathways inside cells normally function and how they go awry to cause disease. This is the insights into the workings of living organisms, fueled by the application of powerful, new technologies.”

—DAVID HARRIS, MD, PHD, professor and chair, Department of Biochemistry

on in one place and not in another,” Dr. Perissi explains. “This is done at the level of DNA where you have a large number of proteins called ‘transcription factors’ that bind to the DNA and determine whether the gene is turned on or not, which is called gene expression.” Dr. Perissi is studying a particular gene involved in keeping the cell’s inflammatory response turned off, which is important because overactivation of the inflammatory response is involved in obesity, diabetes, cancer, and cardiovascular disease. “I am interested in why the body cannot keep the inflammatory response under control with these diseases so that in the future we can design ways to modulate the response and keep it under control.”

Dr. Perissi is delighted to be a part of BUSM: “I feel lucky to have a position here. There is a great deal of communication within and between departments. It is striking how open people are to talk and collaborate, helping me with my lab or with a grant. This was one of the things that weighed heavily in my decision to come to BU.”

Dr. Varelas, who came from the Samuel Lunenfeld Research Institute of the University of Toronto, examines the molecular mechanisms by which cells coordinate growth with cell fate during development and the onset of disease. “We are particularly interested in the role of the Hippo pathway, which is the major pathway regulating cell fate, growth, proliferation, and death,” he says. “If we understand the normal mechanisms or the signaling that determine these processes, we can better understand what happens when they are dysregulated, causing a variety of diseases.”

Dr. Garcia-Marcos, who is from the Basque region of Spain and did his post-doctoral training at the University of California, San Diego, came to BUSM to establish his lab and develop his own ideas. “It is exciting to have this balance here of senior people with a lot of experience and newer scientists with presumably new ideas,” he says. “Doors are open and you are always welcome to talk about anything.”

Dr. Garcia-Marcos has discovered a novel mechanism by which G proteins are regulated and has found that dysregulation of molecular components of the mechanism is involved in the development of cancer metastasis. He hopes to develop new therapeutic strategies for targeting cancer metastasis through research of the G protein regulatory mechanism and is also looking at what other proteins

interact with G proteins to make them more or less active. “The G proteins are involved in so many processes in the body that if something goes wrong with them, there is a very good chance that diseases arise,” he explains.

Organic chemist and one of the senior department members, Catherine Costello, PhD, is a professor of biochemistry, biophysics, and chemistry and director of the Center for Biomedical Mass Spectrometry at BUSM. Internationally recognized for her contributions to proteomics sciences and mass spectrometry, Dr. Costello focuses on determinations of the structures and functions of biopolymers, with emphasis on mass spectrometry-based methods for studies of glycobiology, post-translational modifications of proteins, cardiovascular disease, and protein folding disorders.

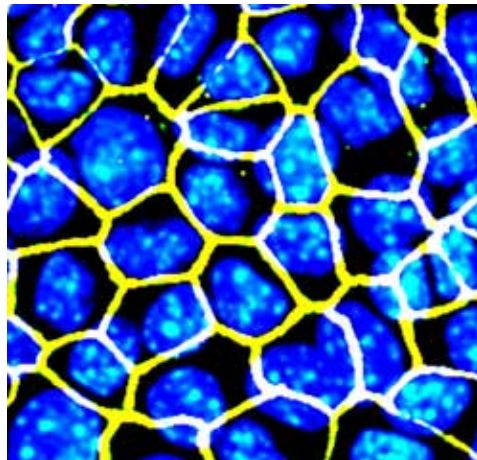
Matthew Nugent, PhD, professor of biochemistry, biomedical engineering, and ophthalmology and a 20-year member of the department, says, “To a large degree, doctoral student training drives research within the department, and as such, this has helped us maintain a rich academic environment that promotes creativity.” Dr. Nugent, also director of the Massachusetts Lions Eye Research Laboratory at BUSM, researches how signaling

molecules called growth factors are controlled in the extracellular space. In particular, his lab is investigating how interactions with compounds naturally found in the weblike gel that holds cells together, called the extracellular matrix, are able to direct growth factor activity.

“Cells within multicellular organisms, like humans, need constant instruction to tell them what to do,” says Nugent. “As such, cells need to be in constant communication with one another in order to coordinate tissue, organ, and organism-wide responses to changing conditions. A large class of proteins called ‘growth factors’ act from outside cells to relay information regarding the status of the tissue,

organ, etc. Under normal conditions, when there has been an injury or infection in a tissue, the cells will respond to repair the damage. However, when these communication systems break down, disease ensues.”

In addition to chairing the department, Dr. Harris is an active scientist who works on neurodegenerative diseases, including Alzheimer’s, and prion diseases which are infectious disorders related to mad cow disease. All are caused by abnormal proteins in the brain.



Normal mammary epithelial cells with their nuclei depicted in blue and cell contact-regulated polarity proteins highlighted in yellow. A common feature associated with tumor-initiation is the deregulation of polarity proteins. Varelas’s work is focused on understanding the mechanisms controlling these proteins and how they contribute to tumor suppression.



Biochemistry Department Chair David Harris (first row L-R) with Valentina Perissi, Stephen Farmer, Brigitte Ritter; (back row L-R) Matthew Nugent, Mikel Garcia-Marcos, and Xaralabos Varelas.

department picnic in the summer. Dr. Harris has also instituted an annual retreat focused on faculty research that has led to the initiation of a series of special interest groups, which are collections of faculty laboratories working on common themes that meet regularly to discuss data and ideas. There is also a Joint Thematic Seminar Series each semester in collaboration with the Evans Center in the Department of Medicine. Each series is based on a single, cutting-edge, scientific theme that bridges basic science and disease, the most recent being “Mitochondria: Engines of Life, Drivers of Disease” in the spring of 2012.

The addition of major equipment has given department members access to state-of-the-art scientific resources to further their research.

The family of a BUSM alumnus has recently made a generous endowment gift to the department that will be used to support new initiatives with a direct impact on students and faculty. This year, the gift was used to establish a fellowship program that provides stipends to two biochemistry graduate students.

“We work in an intellectually vibrant and intensely collegial environment in this department, and we are committed to our students and to supporting and growing the research potential and discoveries of our scientists,” says Dr. Harris. “This department is on the move, making contributions to basic science knowledge that can be translated into clinical applications for disease treatment, and hopefully, disease cures.” ■

From an administrative and operational standpoint, the department has made great strides in the past several years. Major changes to the department’s laboratory space include the complete renovation of approximately 30,000 square feet on three floors of the Silvio Conte Building to provide an open lab plan, allowing for more efficient space utilization and enhanced interactions among researchers. Dedicated rooms for large equipment, tissue culture, microscopes, and film handling, as well as common break areas for informal gatherings, have been created. A seminar room, eating area, and autoclaving facilities are now available, as well as renovated office space for faculty and administration. Two additional floors are slated for renovation in the near future.

Barbara Schreiber, PhD, associate professor of biochemistry and director of graduate studies for the department, has been part of the Medical Campus for more than 35 years, originally as a graduate student in the Department of Microbiology, then as a post-doc, first in clinical microbiology at University Hospital (forerunner to Boston Medical Center) and then with Carl Franzblau, PhD, then-chair of biochemistry. Franzblau offered Schreiber a faculty position and she never left. “Our new young faculty have added an energy and exuberance that has our students flocking to them and vying for positions in their labs,” Dr. Schreiber reports. “Our new monthly seminar series where students and post-docs give presentations to help hone their skills in public speaking has been a wonderful addition. We have launched a completely new website that highlights and markets the strengths of our department.”

Biochemistry department faculty have played a leading role in creating a new program, Foundations in Biomedical Sciences (FiBS), an intense science curriculum that covers biochemistry, cell and molecular biology, genetics, and physiology. The program is a success, with approximately 45 doctoral students enrolled throughout the campus. According to Dr. Schreiber, the Division of Graduate Medical Sciences (with strong support from the Department of Biochemistry) is examining the possibility of a unified admissions process where students are accepted into an umbrella program rather than through a specific department. “The FiBS curriculum is a good first step toward a core curriculum for all doctoral students,” she says. Students will benefit from having a greater pool of faculty mentors from which to choose, as they can rotate through various labs before choosing a thesis advisor. They will also have opportunities to interact with more students. The faculty will benefit from the elimination of duplicated efforts in admissions and student affairs.

Other department-wide initiatives include a monthly “chalk talk” series to give faculty the opportunity to share scientific ideas and get input from colleagues; a weekly social hour with rotating faculty hosts; and an annual

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